

Art Unit: 1623

### EXAMINER'S AMENDMENT

An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Mr. Jay Cinamon on November 04, 2010.

In the Claims of 8/02/2010:

In Claim 1, line 8, after the term "bond" before ".", inserted ", with an esterification degree of the carboxyl of 6.8% to 22% (w/w) and wherein the average molecular weight of hyaluronic acid is 39,000 Da to 200,000Da"

Claims 4, 5, 6, 34, 37 and 38 have been cancelled.

Claims 14-16, 21-25, 27-31, 56-68, 71-73, 82-83, and 85-86 (previously withdrawn) are cancelled.

According to Applicants withdrawn Claims 14-16, 21-25, 27-31, 56-68, 71-73, 82-83, and 85-86 have been cancelled without prejudice and subject to applicant's right to pursue the subject matter of these claims in a continuation application.

### REASONS FOR ALLOWANCE

The following is an examiner's statement of reasons for allowance:

1. Luo et al teach taxane-adipic dihydrazide-hyaluronic acid conjugate in which the hyaluronic acid is attached via a hydrazide bond ( $-\text{C}(=\text{O})-\text{NH}-\text{NH}-\text{C}(=\text{O})-$ ). This conjugate according to Luo is fivefold less effective than free Taxol.
2. Sparer teaches in general about drug-glycosaminoglycan complexes and the desirability to design a drug release system to obtain zero order release to fit the dosage regimen and this may be possible by selecting a given polymer drug bond. There is no suggestion to make a conjugate of Taxol and hyaluronic acid wherein the polymer-drug bond is specifically the ester bond in order to make it more effective than free Taxol.
3. Both Desai et al and Li et al do not exemplify or suggest conjugates of Taxol and hyaluronic acid as instantly claimed.
4. The instant claims (see amended claim 1 in Examiner's amendment above) are drawn to conjugates of Taxol, hyaluronic acid and a spacer wherein the bond between the carboxyl of the hyaluronic acid and the spacer is an ester bond and wherein the degree of esterification is between 6.8%-22% and wherein the molecular weight of hyaluronic acid is between 39,000-200,000Da, the process of preparation of such conjugates and the method of treating tumors via administration of the said conjugates. Applicants have shown that the instant conjugates (see Declaration of Zanellato filed 4/18/2008) are at least 40 times more active than free Taxol. This result is unexpected. Therefore, the instant claims are not rendered obvious by the teachings of the prior art.

Art Unit: 1623

Any comments considered necessary by the applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance".

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ganapathy Krishnan whose telephone number is 571-272-0654. The examiner can normally be reached on 8.30am-5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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Examiner, Art Unit 1623

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Art Unit 1623